UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/581,295	06/01/2006	Sudhir Paul	D6813	3691

7590 05/21/2009

Benjamin A. Adler, PhD, JD
8011 Candle Ln.
Houston, TX 77071

EXAMINER	
PENG, BO	
ART UNIT	PAPER NUMBER
1648	
MAIL DATE	DELIVERY MODE
05/21/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/581,295	PAUL, SUDHIR	
	Examiner	Art Unit	
	BO PENG	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 June 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/6/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *attachement*.

DETAILED ACTION

Restriction election

1. Applicant's election with traverse of Group I (Claims 1-50, insofar as drawn to the special technical feature of an antibody or fragment thereof that binds to Gln-Ile-Lys-Asn-Phe-Leu-Lys-Glu-Val-Gly-Lys-Val-Val-Tyr-Ile), in the reply filed on August 20, 2008, is acknowledged.

2. Applicant traverses the restriction between Groups I and II on the following three grounds: First, the antigen sequences of both Groups I and II are encoded by human endogenous retroviral (HERV) expressed in lupus patients. Specifically, the Group I sequence is encoded by a HERV with GenBank No. AL592563.7, and the Group II sequence is encoded by a HERV with GenBank No. AL391989.9. Second, the antigen sequences of both Groups I and II are homologous to the same HIV gp120 epitope composed of residues 421-436. Third, after binding to the epitope, antibodies to both Groups I and II sequences have the same functional consequence, i.e., the antibodies will interfere with the binding of HIV to the host CD4. Therefore, Applicant requests to rejoin Group II with Group I.

3. Applicant's arguments have been considered, but found not convincing for the following reasons: The claimed antibodies of Groups I and II appear to be different antibodies because they appear to react with different HERV antigens as Applicant indicated. The antibody of Group I binds to HERV antigen fragment Gln-Ile-Lys-Asn-Phe-Leu-Lys-Glu-Val-Gly-Lys-Val-Val-Tyr-Ile (GenBank No. AL592563.7), while the antibody of Group II binds to HERV antigen fragment Lys-Gly-Gly-Lys-Ala-Thr-Tyr-Ser (GenBank No. AL391989.9). These two antigens do not share substantially the same sequence. In addition, these species are not obvious variants

of each other based on the current record. Thus, the antibodies of Groups I and II are different products, and have different special technical features. If applicant is willing to admit that these two antibodies are not patentably distinct, then the various peptides can be rejoined. The requirement is still deemed proper and is therefore made FINAL.

4. Accordingly, Claims 1-50 are pending and are considered in this Office action. Claims 1-50 read on an antibody or fragment thereof that binds to Gln-Ile-Lys-Asn-Phe-Leu-Lys-Glu-Val-Gly-Lys-Val-Val-Tyr-Ile.

Specification

5. The specification and Drawings are objected to for failing to adhere to the requirements of the sequence rules. Applicant must append SEQ ID Nos. to all mentions of specific amino acid sequences comprising four or more amino acids and ten or more nucleic acids in the specification. Specific examples within the specification that do not comply with the sequence rules are found on pages 6 and 24-26, and Figs. 2, 5 and 10. Applicant is required to append a SEQ ID No: to any unidentified sequence within the disclosure that is applicable to the rule. See 37 CFR § 1.821 (a)-(d) and MPEP § 2422.

6. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP §608.01. See [0142] and [0214], for example.

Information Disclosure Statement

7. The information disclosure statement submitted on February 6, 2007, is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

Claims Objections

8. Claims 1 and 2 recite that "a monoclonal antibody.... neutralizes microbial infection". However, an antibody is known to neutralize a pathogen, but not "neutralizes microbial infection". Appropriate correction is required.

Claim Rejections - 35 USC § 112, second paragraph

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 36, 40 and 50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

11. Claims 36, 40 and 50 are indefinite because they refer HERV sequences to the GenBank accession number rather than to sequences set forth in the specification. This is seen as an improper incorporation by reference, since the information required to describe and enable the required sequences is found in the GenBank database, extraneous to the application. Furthermore, since GenBank sequences are not irrevocably fixed but are corrected and updated as additional sequence information becomes available, the GenBank accession number may refer to sequences which change after the application filing date. Deleting references to the GenBank

accession numbers and instead referring HERV sequences to specific SEQ ID Nos: would overcome this rejection.

Claim Rejections - 35 USC § 101 Utility

12. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

13. Claims 1-7, 15, 26-28 and 47-50 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. "antibody fragment" of the claims is a product present in a patient with autoimmune disease, so they are a product of nature. Products of nature do not constitute patentable subject matter under 35 U.S.C. § 101. Amending the claims to "an isolated attenuated mutant" and/or "a purified attenuated mutant" would overcome this rejection.

Claim Rejections - 35 USC § 112, first paragraph-scope of embalmment

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 1-50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had

possession of the claimed invention.

In making a determination as to whether a claimed invention has been adequately described, the courts have identified certain elements that may be considered. Among those elements are the knowledge in the particular field, the extent and content of the prior art, the maturity of the technology, and predictability of the aspect at issue. See e.g., *Capon v. Eshhar*, 76 U.S.P.Q. 2d 1078, at 1085 (CAFC 2005). For a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, **where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...**") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

16. Claims 1-50 are directed a monoclonal antibody or fragment from any organism with any autoimmune disease which **recognizes** a microbial antigen and **neutralizes** any microbial infection. The scope of the claims encompasses **a subgenus** of a monoclonal antibody or fragment, from a genus of monoclonal antibodies or fragments thereof to recognize a microbial pathogen, which both **recognizes** a microbial antigen and **neutralizes** a microbial pathogen. In supporting the claims, the specification has disclosed that a few antibody fragments that recognize residues 421-436 of HIV gp120 (CD4 binding site), and also recognize (cross-react with) HERV antigens (human endogenous virus) isolated from lymphoid cells of lupus patients. However, the specification has not presented any antibody or fragment thereof, which both

recognizes and **neutralizes** any microbial pathogens other than HIV.

17. The art indicates there are uncertainties regarding the operability of an antibody that both recognizes and neutralizes a microbial pathogen. There is no correlation between the ability of an antibody to bind an antigen of a pathogen and its ability to neutralize the pathogen. For example of HIV, Nara teaches that most of antibodies raised against the HIV envelope glycoprotein during natural infection or after vaccination with gp120 subunits are no neutralizing. Binding to particles or env-expressing cells was not sufficient for antibodies to neutralize the virus. These studies suggest that antibodies can successfully bind virions but are unable to inhibit viral entry and infection. See discussion in section "Neutralizing Antibodies", p. 161, Nara, P. *et al.* (Curr Drug Targets Infect Disord. 2005 Jun;5(2):157-70). More examples, Roben P *et al.* teach that human recombinant antibody Fab fragments to the CD4 binding site of gp120 show differing abilities to neutralize HIV-1, see whole document, and Abstract. (J. Virol. 1994 Aug;68(8):4821-8). Thus, the state of the art teaches that it is unpredictable **which** antibody can both recognize and neutralize a pathogen, such as HIV. The instant specification has failed to address such uncertainty, i.e., indicating which antibodies can both bind and neutralize HIV. The specification has also failed to describe a sufficient number of representative species of antibodies for the subgenus of antibodies that both recognizes and neutralizes microbial pathogens.

18. In view of the scope of the claims, and given the unpredictability in performance of the claimed antibodies with the abilities to both recognize and **neutralize** a microbial pathogen, one of ordinary skill in the art would not know **which** of the claimed antibodies have the functional characteristics recited in the claims. Consequently, while the skilled artisan would reasonably conclude that the Applicant was in possession of a few specific antibodies that can

recognize residues 421-436 of HIV gp120 and cross-react with HERV antigens, there is no indication that the Applicant was in possession of the subgenus of antibodies that can both recognize and neutralize any microbial pathogens as broadly claimed.

Claim Rejections - 35 USC § 102

19. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

20. Claims 1-8, 15-23, 26-29, 38, 39 and 47- 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Paul, *et al.* (6,156,541, cited in IDS), as evidenced by Gorny MK *et al.* (J. Virology, 76(18):9035-9045).

21. Claims 1-8, 15-23, 26-29, 38, 39 and 47-49 are directed to a monoclonal antibody, or fragment thereof, from an organism with an autoimmune disease, which **recognizes** a microbial antigen and **neutralizes** a microbial infection, wherein the autoimmune disease is systemic lupus erythematosus (SLE), wherein the antibody or fragment neutralizes HIV-1, wherein the antibody or fragment recognize/bind to an antigen of HIV gp120, or gp120 fragment, wherein the antibody fragment is a Fab fragment, a Fv fragment, a light chain. Claims **18, 19, 22 and 23** require that said antibody or antibody fragment neutralize at least two or three HIV strains belong to different HIV clades.

22. Claim Construction: It is noted that the claims recite the claimed antibody is obtained by a variety of methods. Specifically, Claim 1, 5 and 26 recite the antibody is obtained from a

patient with autoimmune diseases, specifically SLE. Claims 17 and 21 recite the antibody that is obtained by expressing a library of light chain on the surface of phage particles and isolating a subpopulation of Fv particles that bind gp120. Claim 29 recites that the antibody fragment is obtained by cloning cDNA from mDNA expressed by lymphoid cells. Claim 49 recites that the antibody is obtained by screening cell lines derived from lymphoid cells. However, note that based on the MPEP and the definition of "antibody" in the art, the patentability of an antibody is determined by the specificity of the antibody, not by the methods of obtaining the claimed antibody. The methods of obtaining the claimed antibody do not constitute a limitation to the claimed antibody or a fragment thereof. The explanation is set forth below: The following is a recitation from MPEP 2113, and a definition of antibody form The Illustrated Dictionary of Immunology.

"[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) See MPEP § § 2183- 21.

"Antibodies are glycoprotein substances produced by B lymphoid cells in response to stimulation with an immunogen. Antibodies possess the ability to **react specifically and selectively with the antigenic determinant or epitope** eliciting their production or **with an antigenic determinant closely related to the homologous antigen**" (The Illustrated Dictionary of Immunology (1995, CRC Press, Inc. Boca Raton FL; JM Cruse and RE Lewis eds., See attachment to the Office action) (See the attachment to the Office action)

Thus, according to the cited MPEP section, the patentability of the claimed mAb is determined by the antibody itself, not by its method of production. The methods of obtaining the claimed antibody recited in the claims do not constitute either a structural or functional limitation to the

claimed antibody or fragment thereof. Based on the definition of an antibody, the specific antibody is determined by its ability to react with a specific antigen or with an antigenic determinant closely related to the homologous antigen, not by the methods of making the antibody. The claimed antibody fragment, obtained either from a patient with an autoimmune disease (e.g. Claims 1-4), or from a cloning cDNA library (e.g. Claim 17), appears to have the same functional property (specificity) of recognizing and neutralizing HIV, and specifically binding to HIV gp120.

23. Paul teaches that the monoclonal light chain isolated from patients with systemic lupus erythematosus (SLE) can neutralize HIV-1 gp120 (whole document, see e.g. Example III, col. 8). The antibody fragment can be Fab fragments, Fv fragments, light chains and light chain dimers (see claims). The antibody fragment can also be made by cDNA cloning (Example II, col. 7).

24. Furthermore, the monoclonal light chain against HIV-1 gp120 of the prior art inherently has ability to neutralize more than two strains of different HIV clades. By definition, an antibody has the ability to cross-react with "an antigenic determinant closely related to the homologous antigen". As evidenced, Gorny teaches that monoclonal antibodies to HIV gp120 show cross-clade binding to native, intact HIV virions of Clades A, B, C, D and F, See e.g. Abstract, and Para 1-2, right col. p. 9042. Thus, the monoclonal light chain against HIV-1 gp120 inherently has ability to neutralize more than two strains of different HIV clades. In view of these teachings, the instant claims are anticipated by Paul.

102/103 REJECTION

25. Claims 1-8, 15-23, 15-23, 26-29, 36-42 and 47-50 are rejected under 35 U.S.C. 102(b) as

being anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Chang (US 6,309,880, issued Oct. 30, 2002), as evidenced by Gorny MK *et al.* (J. Virology, 76(18):9035-9045), further evidenced by Bost (Immunological Investigations, 17(6&7):577-586, 1988), Golding, H. *et al.* J. Exp. Med., Mar 1988; 167: 914 – 923; and Langat DK, *et al.* (J Reprod Immunol. 1999 Jan;42(1):41-58).

26. Claims **1-8, 15-23, 26-29, 38, 39 and 47- 49** are summarized above. Claims **36, 40-42 and 50** are directed to the antibody fragment, obtained by expressing a library of Fv constructs on the surface of phage particles and isolating a subpopulation of HIV-reactive Fv particles that **an antigen selected from the group consisting of intact HIV, trimeric gp120, monomeric full-length gp120 and peptide fragments of gp120** (see e.g. Claims 17 and 20), wherein the antibody fragment bind Gln-Ile-Lys-Asn-Phe-Leu-Lys-Glu-Val-Gly-Lys-Val-Val-Tyr-Ile (or **QIKNFLKEVGKVVYI**, in single amino acid code), **or fragments thereof**, which correspond to the HERV sequence fragment (Claims 36, 40 and 50).

Claim Construction: The Court indicates:

"The construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be, in the end, the correct construction." Renishaw PLC v. Marposs Societa' per Azioni, 158 F.3d 1243, 1250, 48 USPQ2d 1117, 1122 (Fed. Cir. 1998). The "specification "is always highly relevant to the claim construction analysis. Usually it is dispositive; it is the best single guide to the meaning of a disputed term."" Phillips v. AWH Corp., 415 F.3d 1303, 1315, 75 USPQ2d 1321, 1327 (Fed. Cir. 2005), Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed. Cir. 1996).

In the present case, the specification teaches that the claimed antibody was selected in DNA library form lupus patient (which encodes HERV antigens) by its ability to bind HIV gp120 epitope KQIINMWQKVGKAMYAP (gp120 421-436), See specification, p.26, line 10-34. The specification also teaches that gp120 421-436 share homogenous sequence with HERV antigen

QIKNFLKEVGKVVYI, see p. 7 and 8, and Fig2 and Table 1. Thus, in light of the specification, the instant claims encompass the antibody that specifically binds to HIV gp120 (a.a. 421-436) **I**I**N**MWQK**VGK**AM**Y**AP SEQ ID NO: 1, wherein the antibody also bind QIKNFLKEVGKVVYI, or fragments thereof, which correspond to the HERV sequence fragment.

27. Chang teaches **neutralizing** antibodies or antibody fragment that binds an epitope **I**I**N**MWQK**VGK**AM**Y**AP SEQ ID NO: 1, corresponding to residues 423-437 of HIV gp120, see e.g. l. 39-52, col. 2; and line 19-25, col. 5. Chang teaches that this epitope is highly conserved among HIV-1 strains and isolates; consequently, an antibody specific for one or more of these epitopes can inhibit diverse strains and isolates of HIV-1, see e.g. Example 1, col. 9-11. Chang also teaches construction of chimeric antibodies by chimeric DNA constructs; see e.g. col. 3 and 4; and claims.

28. The relevance of Gorny is set forth *supra* in Para 24.

29. It is noted that Chang's SEQ ID NO: 1 shares 100% homology with the HIV antigen epitope used to select the claimed antibody fragment, and share 5 amino acid residues with HERV antigen fragment recited in the claims 36, 40 and 50, See the sequence alignment below:

```
     IINMWQKVGKAMYAP   SEQ ID NO: 1, Chang
   KQIINMWQKVGKAMYAP   epitope used to select the claimed Ab


                       Chang
 IINMWQKVGKAMYAP  SEQ ID NO: 1 (CD4 binding domain of gp120)
  | |    |||  |
QIKNFLKEVGKVVYI   HERV antigen of the instant Claims
```

30. Chang's antibody appears to have same specificity as the claimed antibody for following reasons: First, the instant claims encompass the antibody of the prior art, which specifically binds

to HIV gp120 (a.a. 421-436) IINMWQKVGKAMYAP SEQ ID NO: 1.

31. Secondly, by definition, "Antibodies possess the ability to react specifically and selectively with the antigenic determinant or epitope eliciting their production or **with an antigenic determinant closely related to the homologous antigen**". Chang's antibody to HIV gp120 (a.a. 421-436) has ability to cross-react with other "with an antigenic determinant closely related to the homologous antigen" by definition. It is also well known in the art that an antibody has the ability to recognize or bind, or cross react with more than one protein that share a homologous sequence. For example, **Bost** *et al.* describes antibodies which bind specifically with IL-2 and HIV envelope protein, due to the presence of a homologous sequence in each protein in which 4 of 6 residues were identical (see entire document, but especially the Abstract and Discussion). Antibodies which bind either the HIV or IL-2 derived sequence do not cross-react with irrelevant peptides (e.g., "Results, page 579). Similarly, **Golding,** H. *et al.* teaches that monoclonal antibodies against the HIV gp41-derived peptide and patients' sera cross-react with native HLA class II antigens, due to their epitopes having a homologous region of five amino acids, see e.g. Fig. 1, p. 916. In addition, **Langat** DK, *et al.* shows that antibodies to HIV gp120 cross-react with endogenous retroviral (ERV) particles in normal primate placental tissues see e.g. Abstract, and Para 1, p. 43.

32. Finally, Chang's antibody must inherently recognize and bind or cross-react with the HERV antigen fragment of the instant claim. The specification teaches that antibody fragments that bind epitope KQIINMWQKVGKAMYAP (gp120 421-436), which is identical to SEQ ID NO: 1, cross-react with HERV antigen, see specification, see p. 7 and 8, and Fig. 2 and Table 1. It is noted that Applicant also indicated on the record that the claimed antibody recognized

HERV sequence encoded by Genback NO.AL592563.7, which share homogenous sequence with residues 421-436 of gp120, see Remarks, p. 2, in the reply filed August 290, 2008. Thus, Chang's antibody to IINMWQKVGKAMYAP (SEQ ID NO: 1) must recognize and bind the HERV antigen of the instant claims.

33. Thus, in view of the scope of the claims, considering antibodies cross react with proteins which share a homology sequence, and equivalent antibody products that can be obtained by multiple routes, the antibody disclosed in the prior art appears to be the same antibody or obvious variants as the claimed antibody or antibody fragment thereof, since they appear to have the same specificity. The burden is on the applicant to establish a patentable distinction between the claimed and referenced antibodies. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald *et al.*, 205 USPQ 594 (CCPA 1980).

Claim Rejections - 35 USC § 103

34. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

35. Claims 36, 37, 40, 41 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Paul S. (6,156,541, '541), as evidenced by Gorny MK *et al.* (J. Virology, 76(18):9035-9045), as applied to Claims 1-8, 15-23, 26-29, 38, 39 and 47-49 above, further in view of Chang (US 6,309,880), Pau S *et al.* (2) (Appl. Biochem Biotechnol. 2000, Jan-Mar; 83(1-3),

00.71-82, cited in IDS), Bost (Immunological Investigations, 17(6&7):577-586, 1988), Golding, H. *et al.* (J. Exp. Med., Mar 1988; 167: 914 – 923); and Langat DK, *et al.* (J Reprod Immunol. 1999 Jan;42(1):41-58).

36. The relevance of Paul ('541) is set forth *supra*. However, Paul does not explicitly teach the antibody fragments that can bind HERV antigen **QIKNFLKEVGKVVYI**.

37. Paul (2) teaches that monoclonal light chains (L chains) from multiple myeloma patients have the ability to cleave HIV gp120, see e.g. Abstract. Paul teaches that gp120 isolated from strains SF2, MN, and IIIB were cleaved by the antibody L chain. Thus, Paul suggests that the substrate recognition determinants (antigens or epitopes) in gp120 may be conserved in different HIV-1 strains. Paul explicitly suggests utilizing gp120-cleaving antibodies in the treatment of AIDS, see Abstract.

38. The relevance of Clang is set forth *supra*, See Para 27-30. Specifically, Chang teaches an antibody that bind to gp120 SEQ ID NO: 1, which share homogenous residues with HERV antigen **QIKNFLKEVGKVVYI**.

39. The relevance of Gorny is set forth *supra* in Para 24.

40. The relevance of **Bost**, **Golding**, and **Langat** DK, *et al.* are set forth *supra*.

41. It would have been obvious to the ordinary artisan to isolate/make an antibody form SLE patients that can recognize the HIV, as an alternative or an equivalent, for treatment of AIDS as taught by Paul and Chang. The skilled artisan would have been motivated to do so given the suggestion by Paul (1) and (2) that a catalytic antibody in SLE patient can cleave HIVgp120. They would have a reasonable expectation of success in obtaining an antibody which cross-reacts with gp120 and HERV antigen, given the knowledge that substrate recognition

determinants of monoclonal light chains obtained from SLE patients is conserved in different HIV-1 strains, as taught by Paul (2), given the knowledge that CD4 binding site of gp120 (a. a. 421-436) **I**IN**M**WQ**K**V**GK**A**M**Y**A**P SEQ ID NO: 1 is highly conversed in HIV strains, as taught by Chang, and also given the knowledge that antibodies can "cross-react" with different antigens that share as few as a 4-residue sequence in each antigen, as taught by Bost. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

41. Claims 9-14, 24, 25, 30-35 and 42-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Paul S. (6,156,541), Chang (US 6,309,880), Pau S *et al* (2), Bost, Golding, and Langat DK, as applied to Claims 1-8, 15-23, 26-29, 36-41 and 47- 50 above, and further in view of Kriangkum (Biomolecular Engineering 18:31-40, 2000).

42. Claims 11-14, 24, 25, 30-35 and 41-46 require the antibody fragment is a recombinant single-chain Fv construct.

43. The relevance of Paul ('541) is set forth *supra*. However, Paul ('541) does not explicitly teach the embodiments of **single chain Fv** constructs as recited in Claims 11-14, 24, 25, 30-35 and 41-46 .

44. The relevance of Paul (2) is set forth *supra*. Moreover, Paul (2) suggests that "The specificity of gp120 cleavage can be enhanced by linking the catalytic V_L domain to a V_H domain that binds gp120, see e.g. Para 1, p. 81. Paul teaches that anti-VIP Fv constructs

containing a catalytic V_L domain linked to a VIP binding V_H domain has improved VIP binding affinity and catalytic efficiency.

45. The relevance of Gorny, Bost, Golding, and Langat DK, *et al.* are set forth *supra.*

46. Kriangkum provides teachings indicating that constructing a single chain Fv is widely used in the art of antibody to enhance antibody function. Specifically, Kriangkum teaches that in single chain Fv constructs, variable domains of heavy and light chains are joined together with a linker to form a single polypeptide chain. Recombinant antibodies have been further altered by genetic fusion with ligands or biologically active molecules resulting in the formation of bifunctional antibodies. Alternatively, fusion of two different antibodies gives rise to the formation of bispecific antibodies; see e.g. right col. p. 31.

47. It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the single chain Fv of the monoclonal light chain from patients with systemic lupus erythematosus (SLE) as suggested and taught by Paul (2) and Kriangkum. The skilled artisan would have been motivated to do so, and would have a reasonable expectation of success, given the knowledge that anti-VIP Fv constructs containing a catalytic V_L domain linked to a VIP binding V_H domain has improved VIP binding affinity and catalytic efficiency as taught by Paul (2), and also given the knowledge that the strategies for making a single chain Fv as detailed by Kriangkum. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

48. Claims 1-10, 15-17, 21, 26-28, 38, 39 and 47-49 are rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1-8 of U.S. Patent No. 6,156,541 ('541). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant application are anticipated by Claims 1-8 of '541.

49. Claims 1-8 of '541 are directed to an isolated natural occurring, catalytic antibody obtained from a patient with SLE, wherein the antibody consists of Fab fragments, Fv fragments, light chains and light chain dimers.

50. Thus, the subject matter of Claims 1-10, 15-17, 21, 26-28, 38, 39 and 47-49 of the instant application is anticipated by Claims 1-8 of '541.

Remarks

51. No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bo Peng, Ph.D. whose telephone number is 571-272-5542. The examiner can normally be reached on M-F, 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/BO PENG/
Examiner, Art Unit 1648